

IN THE CLAIMS:

This listing of claims will replace all prior versions, and listings, of claims in the application:

1. – 11. (Cancelled).
12. (Original) A method for predicting alternative splicing transcripts using DNA chip expression data, the method comprising:
 - performing test sample preparation and hybridization for a set of tissue samples during which hybridization reactions of the set of tissue samples are scanned;
 - preprocessing data resulting from the scanned hybridization reactions; and
 - performing a first splice variant prediction to produce first splice variant prediction data.
13. (Original) The method of claim 12, further comprising performing a second splice variant prediction to produce second splice-variant prediction data.
14. (Presently amended) The method of claim 12, wherein sample preparation and hybridization comprises:
 - extracting total RNA from the set of tissue samples;
 - preparing double-stranded cDNA from the extracted total RNA;
 - ~~performing phenol-chloroform extraction and ethanol precipitation on the double-stranded cDNA to produce a cDNA reaction;~~
 - ~~using one-half of the cDNA reaction as a template in an in vitro~~ performing a transcription reaction using the cDNA to produce cRNA;
 - purifying and quantifying the cRNA;
 - randomly fragmenting the cRNA;
 - hybridizing the randomly fragmented cRNA; and
 - scanning the results of hybridization.
15. (Original) The method of claim 12, wherein preprocessing data resulting from the scanned hybridization reaction comprises:

extracting raw signal intensity readings of each probe on the DNA chip in the data resulting from the scanned hybridization reaction;

normalizing the extracted raw signal intensity readings by removing noise resulting from background hybridization from the extracted raw signal intensity readings;

performing global scaling on the normalized raw signal intensity readings;

generating a normalized difference table by subtracting each mismatch signal from its corresponding perfect match signal within the normalized and scaled intensity readings; and

generating a normalized ratio table by dividing the perfect match and mismatch signals of each probe pair within the normalized and scaled intensity readings.

16. (Currently Amended) The method of claim 12, wherein performing a first splice variant prediction to produce first splice variant prediction data comprises:

combining a normalized difference table and a normalized ratio table produced by the preprocessing step to generate a signal strength table;

filtering out data in the signal strength table that corresponds to uninformative probes using at least one cut-off threshold;

calculating the average difference of each probe set in each tissue sample;

calculating the average difference of each probe across different tissue samples;

calculating tissue-specific relative signal strength data by normalizing the expression level across tissues in the normalized and thresholded signal strength data; and

~~convert~~ converting the tissue-specific relative signal strength data to a final log ratio.

17. (Original) The method of claim 13, wherein performing a second splice variant prediction to produce second splice-variant prediction data comprises sorting splice variant prediction data generated by performing a first splice variant prediction to prioritize the data.

18. (New) A computer readable medium having instructions stored thereon which, when executed, cause a computer to perform one or more tasks of the method of claim 12.

19. (New) A method for predicting alternative splicing transcripts using expression profiling data gathered using a number of different probes, comprising:

preprocessing and filtering the expression profiling data to produce normalized

difference and ratio tables based on the difference of probe perfect matches and mismatches and the ratio of probe perfect matches to mismatches, respectively;

combining the difference and ratio tables to generate a signal strength table;

creating a relative signal strength table by normalizing the signal strength table across tissues represented in the expression profiling data;

calculating final ratios indicative of the differential relative expression of the probes in the tissues represented in the expression profiling data using the relative signal strength table;

selecting probes with final ratios higher than a defined threshold; and

predicting selected probes as likely alternative splicing transcripts based on one or more factors selected from the group consisting of location on a gene and proximity to other selected probes.

20. (New) The method of claim 19, wherein the final ratio is a logarithmic ratio.

21. (New) The method of claim 19, wherein combining the difference and ratio tables to create a signal strength table comprises:

creating the signal strength table using the entries in the difference table; and

assigning a default difference value for each probe pair with a ratio in the ratio table of less than a minimum ratio threshold.

22. (New) The method of claim 21, further comprising filtering the signal strength table to remove uninformative probes.

23. (New) The method of claim 22, wherein said filtering comprises replacing entries in the signal strength table that are above or below defined cut-off values with the cut-off values.

24. (New) The method of claim 23, wherein creating the relative signal strength table by normalizing the signal strength table comprises:

calculating the average difference of each probe set represented in the signal strength table in each tissue; and

for each probe set represented in the signal strength table, dividing by the average difference.

25. (New) The method of claim 19, wherein the final ratio is a logarithmic ratio of the relative signal strength of a set of probes in a particular tissue to the average relative strength of the set of probes in all tissues except the particular tissue.

26. (New) The method of claim 19, further comprising outputting a list of the selected probes identified as likely alternative splicing transcripts.

27. (New) A computer-readable medium having instructions stored thereon which, when executed, cause a computer to perform the method of claim 19.

IN THE DRAWINGS:

The attached sheet of drawings includes changes to Figure 5. This sheet replaces the original sheet showing Figure 5. In the replacement sheet of drawings, the applicants have corrected a typographical error by changing the phrase “predication data” in box 2335, which was obviously incorrect, to the correct “prediction data.” Approval of this drawing change is respectfully requested

Attachment: Replacement Sheet.